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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Hubertus Irth

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NORRIS, MCLAUGHLIN & MARCUS, P.A.

875 THIRD AVE

18TH FLOOR

NEW YORK, NY 10022

EXAMINER

SHEN, BIN

ART UNIT

PAPER NUMBER

1657

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/516,441	<b>Applicant(s)</b> IRTH ET AL.	
	<b>Examiner</b> BIN SHEN	<b>Art Unit</b> 1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 21 December 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                      |                                                                   |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____                                                          | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

The amendment received 12/21/2007 has been entered and claims 1-12 are currently pending in this application. The amended abstract is acceptable.

In view of the amended claims, the rejections under 35 USC § 112 first and second paragraph are hereby withdrawn.

Applicant's arguments with regard to the rejections under 35 USC § 102 over Ingkaninan, under 35 USC §103 over Ingkaninan/Bocchini, and Ingkaninan/Edmondson are hereby withdrawn. This action is made non-final due to the new ground of rejection presented below.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 recites the limitation "said enzyme" in line 1. There is insufficient antecedent basis for this limitation in the claim, and "the enzyme" in claim 1, line 4 clearly refer to a enzyme, not more than one enzyme.

Claim 11 recites the limitation "the enzymes" in line 2. There is insufficient antecedent basis for this limitation in the claim.

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-7, 9-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Bu et al. (2000).

Bu et al. teach an on-line detection method for inhibitors of enzymes and their inhibition activity (see Title and abstract), comprising the steps of: contacting a fractionation effluent with

a controlled amount of an enzyme (cytochrome P450); allowing the enzyme to interact with analytes suspected to be present in the fractionation effluent; addition of a controlled amount of a substrate (CYP probe substrate) for the enzyme; allowing a reaction of the enzyme with the substrate providing one or more modified substrate products; and detection of unreacted substrate or a modified substrate product (CYP probe substrates and their marker metabolites, see page 1620, left column, 2<sup>nd</sup> full paragraph, lines 12-13) using a electrospray ionization mass spectrometer (page 1620, right column, 3<sup>rd</sup> full paragraph), wherein a make-up flow is added to the reaction mixture prior to the introduction in the mass spectrometer (using a Phenomenex C<sub>18</sub> guard cartridge, page 1620, right column, 3<sup>rd</sup> full paragraph), wherein the fractionation step is a liquid chromatography separation (page 1620, right column, 3<sup>rd</sup> full paragraph), Wherein said enzyme is a mixture of two or more different types of enzymes (CYP isoforms, see page 1619, left column, 1<sup>st</sup> paragraph).

Therefore, the cited reference is deemed to anticipate the instant claims above.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4, 7, 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bu et al. in view of Bocchini et al. (1999).

Bu et al. teach what is above.

Bu et al. does not teach the passage of the reaction mixture through a hollow-fibre module prior to entering the mass spectrometer.

Bocchini et al. teach the use of a thin polymeric hollow-fibre membrane for the reaction mixture to pass through prior to entering the mass spectrometer (abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the hollow-fibre membrane of Bocchini in the method of Bu because Bocchini teaches the advantages of the technique are that no pretreatment of samples before analysis is needed and that it has fast response times and on-line monitoring capabilities. One would have been motivated to make the modification because Bocchini et al. specifically described the set-up of the system (hollow-fibre module) and the evaluation of the linearity of response, repeatability, detection limits, and spectra quality, and would reasonably have expected success in view of both Bu and Bocchini's teachings.

Claims 1, 2, 4-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bu et al. in view of Edmondson et al. (2002).

Bu et al. teaches what is above.

Bu et al. does not teach the liquid chromatograph separation step is an HPLC, the enzyme is a protein kinase, and a mass spectrometer with a multiple-inlet.

Edmondson et al. teach the use of a ionization mass spectrometry to identify many proteins in Protein Kinase C (PKC)  $\epsilon$  complex (abstract). Edmondson et al. perform a mass spectrometry analysis with fast gradient nanoscale LC/MS/MS with splitting streams (read as multiple-inlet) (page 423, right column 1st full paragraph), and the mixture of peptides (proteins) are analyzed using electrospray tandem mass spectrometers (page 424, left column 1<sup>st</sup> full paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use ionization mass spectrometry to identify multiple enzymes (proteins) in the method of Bu because Edmondson teaches that identifying the protein components of the protein complexes (such as PKC  $\epsilon$ ) is important for understanding its physiological function (abstract and page 421, right column, 1<sup>st</sup> paragraph). One would have been motivated to make the

modification because Edmondson specifically described a mass spectrometry analysis with fast gradient nanoscale LC/MS/MS with splitting streams (read as multiple-inlet) (page 423, right column 1st full paragraph), and the mixture of peptides (proteins) are analyzed using electrospray tandem mass spectrometers (page 424, left column 1<sup>st</sup> full paragraph), and would reasonably have expected success because Edmondson teaches that the method they use is highly sensitive (abstract, lines 16-18). The claim would have been obvious because the substitution of one known element (liquid chromatograph for the phenomenex C<sub>18</sub> guard cartridge as taught by Bu et al.) with a functionally equivalent other (HPLC for example as taught by Edmondson et al.) would have yield predictable results to one of ordinary skill in the art at the time of the invention.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

### ***Conclusion***

No claim is allowed.

Certain papers related to this application may be submitted to Art Unit 1657 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is

(866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Bin Shen, Ph.D., whose telephone number is (571) 272-9040. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to her office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached at (571) 272-0925.

*B Shen*

Art Unit 1657

/Jon P Weber/

Supervisory Patent Examiner, Art Unit 1657